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Effects of oxytocin on women's aggression depend on state anxiety

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Abstract

Research on oxytocin (OT) indicates that it has stress reducing effects. This leads to opposing predictions of decreased and increased aggression which we examine in this study. Following completion of a state anxiety measure and administration of OT or a placebo, female participants took part in a competitive aggression game (PSAP) for a monetary prize which, if won, would be paid to a loved one. In the game, three options were available: Participants could earn points; attack their opponent by deducting points; and defend themselves against point deduction by their opponent. There was no main effect of OT on these responses, however there was an interaction with state anxiety. In the placebo condition, women higher in state anxiety showed a significantly higher ratio of Attack-to-Earn responses than low anxiety women. Under oxytocin, there was a significant reduction in their Attack: Earn ratio resulting in no significant difference between high and low state anxiety groups. There was a similar trend for the Defend: Earn ratio. The reduction of reactive aggression in state anxious women supports the view that OT may decrease negative behaviour and increase constructive behaviour even under conditions of provocation.

Keywords: Oxytocin; aggression; defence; women

Introduction

The neuropeptide oxytocin (OT) has gained a reputation as the ‘bonding’ hormone. In humans and other mammalian species, OT has anxiolytic (stress reducing) effects (Heinrichs, Baumgartner, Kirschbaum, & Ehlert, 2003; Kirsch, Esslinger, Chen, Mier, Lis, Siddhanti, et al., 2005). This stress reduction is thought to underlie increased trust and cooperation found in experimental studies (Baumgartner, Heinrichs, Vonlanthen, Fischbacher, & Fehr, 2008; Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr, 2005). But the surge of interest in OT’s prosocial effects should not occlude investigation of its potentially less desirable consequences (Campbell, 2010). Recent human studies suggest that OT can enhance defensive non-cooperation against an out-group (De Dreu, et al., 2010), decrease cooperation when social information is lacking (DeClerck, Boone, & Kiyonari, 2010), and increase feelings of envy and gloating (Shamay-Tsoory et al., 2009). In the present study, we explore the impact of OT on women’s interpersonal aggression using a well-validated laboratory measure (Cherek, Lane, Dougherty, Moeller, & White, 2000; Cherek, Moeller, Schnapp, & Dougherty, 1997). In the Point Subtraction Aggression Paradigm (PSAP), a game is played against a second player in which the participant can earn points, attack their opponent by subtracting points from them or defend themselves from their opponent’s attacks. Four proposals can be advanced about the possible effects of OT on aggression.

The first is that *OT will reduce aggression*. Suggestive evidence comes from Baumgartner et al.’s (2008) study using the Trust Game in which a participant ‘trustee’ sends money to a second player (‘investor’) which is tripled in value by the experimenter. The investor may choose to return some portion of this money to the trustee. When participants were informed that their trust had been betrayed on 50

percent of occasions, placebo recipients subsequently showed a decline in trusting behaviour. The absence of such a decline among OT participants, suggested that OT maintains trust even in situations that typically engender hostility and retaliation. Also relevant to the aggression reduction hypothesis are studies showing that OT increases affective empathy (Bartz et al., 2010; Singer et al., 2008) which is negatively correlated with aggression (Eisenberg, 2000).

The second hypothesis is that *OT will enhance defence but not attack in women*. Taylor et al. (2000) argue that the fight-or-flight response to threat is characteristic of men rather than women because, in evolutionary terms, attack or flight would jeopardise the lives of mothers and their offspring. When threatened, women quieten their offspring and affiliate for defence. They propose that the anxiolytic effects of OT in women decrease the sympathetic activity necessary for the fight-or-flight response. The tend-and-befriend position suggests that the modal response to threat in women, mediated by OT, will be attempts at self-protection that fall short of aggression. We are able to examine this because the PSAP paradigm distinguishes between non-aggressive defence and aggressive counter-attack.

The third proposal is that *OT increases attack where aggression is the prepotent response*. The paradoxical effects of OT have been taken to suggest that OT acts by increasing the salience of contextual cues (Bartz, Zaki, Bolger, & Ochsner, 2011). OT enhances prosocial behaviour where situational cues indicate positive social interaction, but where situational cues signal possible threat, OT enhances antagonism (Taylor, 2006). Shamay-Tsoory et al. (2009) found that OT increased both gloating (when their partner's winnings were lower than their own) and envy (when the situation was reversed). DeClerck et al. (2010) found that, although OT increased cooperation in a Prisoner's Dilemma when players had previously interacted, without

prior contact OT significantly decreased cooperation. They concluded that “The saliency of the social information becomes crucial in determining the direction in which OT will operate” (p.372). The PSAP paradigm, in which the participant is provoked and has the capability of a punitive response, makes aggression highly salient.

A fourth proposal is that *OT increases defensive aggression*. This derives from a considerable body of animal research on maternal aggression which represents the ‘other side of the coin’ of mother–infant bonding (Debiec, 2005; Pedersen, 2004). Infusion of OT into the central amygdala increases maternal aggression (Ferris et al., 1992) while lesions of the paraventricular nucleus(the site of OT synthesis) decrease it (Consiglio & Lucion, 1996). Increased willingness to attack is mediated by fear reduction (Gammie, Negron, Newman, & Rhodes, 2004). Recent human evidence suggests that breastfeeding women show increased aggression as a function of lowered stress reactivity which may be associated with heightened oxytocin levels during lactation (Hahn-Holbrook, Holt-Lunstad, Holbrook, Coyne, & Lawson, 2011).The core idea---that OT selectively facilitates aggression on behalf of kin or allies---was recently examined in humans by De Dreu et al. (2010). After assignment to a three-person ‘ingroup’, OT selectively increased ingroup trust and monetary allocation.Participants were then told they were representing their group against a member of anothergroup in a game of Prisoner’s Dilemma. OT significantly increased non-cooperation only where likelihood of exploitation by the outgroup was high. The authors conclude that “oxytocin stimulates humans to aggress against out-group threat in order to protect their in-group” (p. 1411).

We qualify the above hypotheses by predicting a significant interaction between OT and state anxiety. In sixty three per cent studies, OT effects are

moderated by situational or individual difference variables (Bartz, et al., 2011). Researchers now recognise the conceptual and clinical importance of identifying those individuals who are most likely to be affected by OT administration. Given the well-established anxiolytic effects of OT, these are likely to be more anxious individuals. In patients with anxiety disorders, OT diminished hyperactivity to fearful facial expressions (Labuschagne, et al., 2010) and, in combination with cognitive behavioural therapy, reduced negative self-appraisals of public speaking (Guastella, Howard, Dadds, Mitchell, & Carson, 2009). In non-clinical populations, oxytocin reduced negative self-appraisals in men high, but not low, in trait anxiety (Alvares, Chen, Balleine, Hickie, & Guastella, 2012). In women, OT selectively reduced anxiety after a stress manipulation only for those high in emotion-oriented coping, indicative of increased stress vulnerability (Cardoso, Linnen, Joobar, & Ellenbogen, 2012).

Anxiety is of particular interest because our study employs a female sample. Sex differences in anxiety are well established (Costa, Terracciano, & McCrae, 2001) and the up-regulation of OT receptors by oestrogen may render females especially sensitive to OT's anxiolytic effects (Akaisha & Sakuma, 1985; Young, Wang, Donaldson, & Rissman, 1998). The vast majority of OT studies have been performed on men. The importance of studying women has been further underlined by recent findings that sexually dimorphic effects of OT. In men, OT depresses amygdala response to threat-related scenes and faces (Domes et al., 2007; Gamer, Zurowski, & Buchel, 2010; Kirsch et al., 2005; Petrovic, Kalisch, Singer, & Dolan, 2008) but two recent studies found that in women, under similar conditions, amygdala activation is increased by OT (Domes et al., 2010; Lischke et al., 2012).

To maintain continuity with a previous study which manipulated ingroup loyalty as the motivation for aggression, we informed participants that the monetary prize for winning the game would be paid not to them but to a loved one whom they would nominate in advance. Our study design therefore bears similarities to De Dreu et al. (2010, Study 3). In that study, relationship loyalty was manipulated by assigning participants to 'ingroups' (composed of strangers) on whose behalf the participant played, whereas we invite participants to act on behalf of their real-world 'ingroup'. In the De Dreu study, threat was manipulated by altering the pay-off matrix of the Prisoner's Dilemma game, while we use provocative point subtractions by a second player. An advantage of the PSAP is that it provides a pure measure of hostile aggression (in which an attack confers no material benefit on the attacker) as well as non-aggressive defence.

Method

Participants and design

The participants were undergraduate women aged between 18 and 21 attending the Durham University (N=45). Participants were informed that this was a study of an administered hormone on a range of social tasks involving another participant. Anonymity was guaranteed. The experiment was approved by the Departmental Ethics Committee. The between-group independent variable was Treatment (placebo versus OT). We used a double-blind, placebo-controlled design, hence neither the researcher nor the participant knew whether they had received OT or placebo. To ensure that any behavioural effects could be unambiguously ascribed to OT, the placebo was manufactured to be visually and chemically identical to the active substance, except that it lacked the neuropeptide. The dependent measures were

the participant's number of earn, attack and defend responses during the Point Subtraction Aggression Paradigm (PSAP).

OT administration and procedures

On arrival at the laboratory, participants completed a health screening questionnaire, self-administered a pregnancy test and confirmed that the result was negative. A written overview of experimental procedure was given to them and they signed a consent form. Participants were informed that they could win £5 depending on the number of points they earned on a game to be played against a second participant. This money would not be paid to them but to a loved one whom they identified, also indicating their relationship to the participant. They were asked to address an envelope to the loved one that could be used to mail the money if they were successful. They also completed the state anxiety scale of the State-Trait Anxiety Inventory (Spielberger, Gorsuch, & Lushene, 1970). Respondents rated 'how they feel now, at this moment' on a series of 20 adjectives (e.g. nervous, tense, self-confident). The STAXI has been used in over 3,000 studies (Spielberger, 1989), and its construct and convergent validity have been established (e.g. Rule & Travers, 1983; Smeets, Merckelbach, & Griez, 1996). The internal consistency in the present sample was Cronbach's $\alpha = .88$.

Spray bottles containing either OT or a placebo (containing only the carrier and no active ingredient) were assigned to participants using a double blind procedure. They inhaled three puffs through each nostril delivering a total of 24 IU OT. To allow time for OT to diffuse through the subarachnoid space and bind to central receptors, 45 minutes elapsed before they took part in the PSAP (e.g. Born et al., 2002). An experimenter was present in the room throughout this period, supervising their completion of an unrelated paper-and-pencil task. To increase the

participant's belief that they would be interacting with another participant, a second experimenter briefly entered the room and told the experimenter that the 'partner' was ready to commence the PSAP interaction.

Point Subtraction Aggression Paradigm

The program and instructions for the game were based on those described by Cherek, Moeller, Schnapp and Dougherty (1997). Instructions were presented to the participant onscreen with the experimenter present to answer any questions. It was explained that they would be playing against a second participant in another room and the aim was to amass more points than them. To do this, they could choose between three response options. Pressing the Earn button 100 times would earn one point. Their opponent could deduct a point from them at any time and it would be added to the opponent's total. When this occurred, the screen border would briefly turn red and they would see a message saying "Point deducted". The participant was told they could also deduct points from their opponent by pressing the Attack button 10 times, but the opponent's point would not be added to their own total. (This ensured that their aggressive responses were hostile rather than instrumental.) Pressing the Defend button 10 times would protect them from point deduction by their opponent for some period of time. Point subtractions by the opponent were programmed to occur randomly with intervals of between 6 and 120 seconds between successive subtractions. Participants then took part on a 3 minute practice session with the experimenter present to ensure that they understood the task. Following this, they played against an ostensible opponent for 15 minutes. The PC monitor displayed their current score but not that of their opponent.

Results

High and low state anxiety participants

To differentiate between individuals who were low and high in state anxiety, we performed a median split based on their scores on the state anxiety scale that was completed prior to OT administration. Following the median split, an independent t-test confirmed a significant difference in the scores between individuals low in state anxiety (30.75 ± 2.44) and individuals high in state anxiety (41.40 ± 8.15), $t(43) = 5.63$, $p < .001$.

Treatment and state anxiety effects on response options

The focus of the study was the relative time and energy spent in attacking or defending as opposed to earning points during the testing period. We therefore computed two dependent variables for each participant: The ratio of Attack to Earn responses and the ratio of Defend to Earn responses. We performed an analysis of variance for each of these two measures with Treatment (placebo or OT) and Anxiety (high or low) as between group independent variables (see Table 1).

Table 1. Means (and standard deviations) for Attack and Defend ratios as a function of treatment and participant anxiety

Treatment	State Anxiety	Attack ratio ^a	Defend ratio ^b
Placebo	High anxiety	1.66 (1.23)	1.50 (1.38)
	Low anxiety	0.78 (0.35)	0.87 (0.64)
Oxytocin	High anxiety	0.84 (0.53)	0.80 (0.49)
	Low anxiety	1.18 (0.75)	1.22 (0.62)

Note. a. The ratio of Attack responses to Earn responses. b. The ratio of Defend responses to Earn responses.

For Attack ratio, there was no main effect of Treatment, $F(1,41) = 0.64, p = .43$, or Anxiety, $F(1,41) = 1.02, p = .32$. The interaction term was significant, $F(1,41) = 5.20, p = .03$. In the placebo condition, high state anxiety women had a significantly higher Attack ratio than low state anxiety women, $t(23) = -2.69, p < .02$, with a large effect size of $d = 0.97$ (see Figure 1). In the OT condition this difference between high and low state anxiety participants was abolished, $t(18) = 1.15, p = .27$. This was attributable to a significant reduction in Attack ratio for the high state anxiety group only, $t(23) = 2.34, p = .03$, for which the effect size was large, $d = 0.87$. The mean ratio for the high state anxiety group went from a value above unity (indicating more Attack than Earn responses) to a value below unity (fewer Attack than Earn responses).

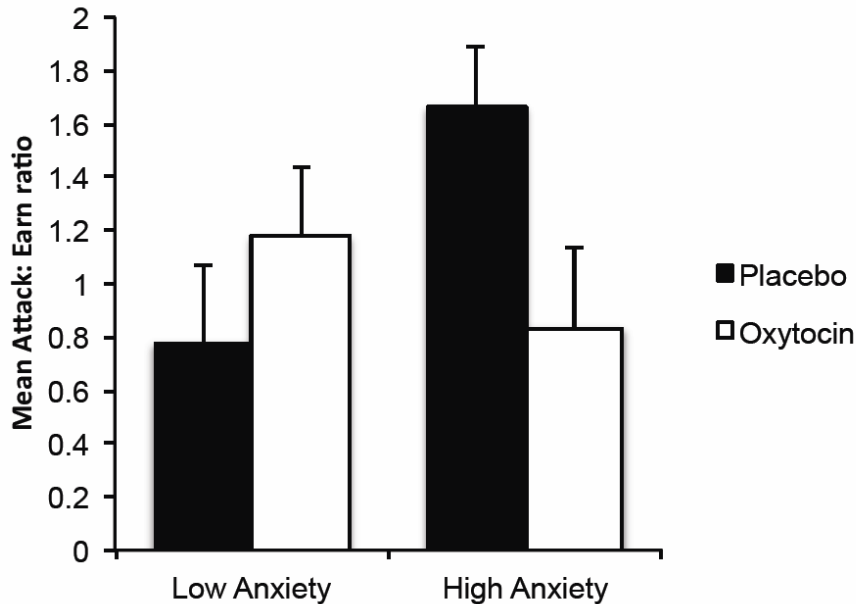


Figure 1. Mean ratio of Attack to Earn responses as a function of state anxiety level and treatment.

For Defend ratio, the main effects were again not significant for either Treatment, $F(1,41) = 0.36, p = .55$, or Anxiety, $F(1,41) = 0.13, p = .72$. The

interaction term only approached significance, $F(1,41) = 3.14, p = .08$. We followed up this interaction with tests of simple effects to see if the results mirrored those found for Attack ratio. The only effect that approached significance was for the high state anxiety group which showed a lower Defend ratio in the OT condition, $t(23) = 1.82, p = .08, d = 0.68$. Similar to the Attack ratio, the mean value for high state anxiety participants in the placebo group indicated more Defend than Earn responses, whereas the OT group showed the reverse pattern.

Discussion

This is the first study to experimentally investigate the effect of OT on aggression. This is surprising because a link between OT and human aggression has been proposed by a number of authors (e.g. Pedersen, 2004; Siever, 2008), based on experiments reporting effects of OT on aggression-related measures such as fear, trust and cooperation. None has directly examined aggression as a dependent variable.

For example, DeDreu et al. (2010, Study 3) found that, under threat of exploitation by an out-group, OT enhanced levels of non-cooperation on a Prisoner's Dilemma game. They described this as "defensive aggression", but non-cooperation falls short of the usual definition of aggression as the infliction of intentional harm or injury (Anderson & Bushman, 2002). Aggression is the active delivery of harm and goes beyond a failure to cooperate motivated by a desire to avoid loss. Closer to this conceptualisation of aggression was the measure used by De Dreu et al. (2010) in Study 1. After assignment to three-person 'ingroups', participants were given €10 to spend. They chose how much of this sum they wanted either to retain for themselves; to contribute to the within-in group pool (every €1 added €0.50 to each in-group member including the contributor); or to contribute to the between-group pool

(the same as for within-group choice but this also subtracted €0.50 from every out-group member). This latter choice, representing “spiteful” out-group behaviour, was analogous to the aggressive option in the present study: In both cases this option disadvantaged another player but did not accrue any material advantage to the participant. However enhanced aggression was not found either by De Dreu et al. (2010) or as a main effect in the present study.

Others have suggested that OT specifically promotes prosocial motivation by reducing interpersonal apprehension as evidenced by greater trust, sensitivity to eye gaze, altruism, empathy, and selective recognition and recall of positive emotional stimuli (see reviews by Campbell 2010; Bartz et al., 2011). This prosocial viewpoint of OT effects is more concordant with the present finding of lowered aggression but with the important caveat that this was true of individuals high, but not low, in state anxiety. Anxious women in the placebo condition exhibited a significantly higher ratio of Attack to Earn against their opponent compared to women lower in state anxiety. This effect was abolished by OT administration. The effect sizes we found were large by Cohen’s criteria (Cohen, 1988) and hence detectable even with our relatively modest sample size. It appears that OT diminishes the hostility typically expressed by highly state anxious individuals in competitive and provoking situations.

The higher ratio of attack by highly anxious women in the control condition is concordant with Eysenck’s (1964) conceptualisation. He proposed that high neuroticism, manifest in a hyper-reactive sympathetic nervous system, is associated with heightened aggression and this has been borne out in a number of studies especially under conditions of provocation associated with angry or hostile aggression (Egan & Lewis, 2011; Jones, Miller & Lynam, 2011). Given that the Attack option in PSAP has no instrumental advantage in terms of gaining points, it constitutes a pure

case of spiteful, reactive aggression that was diminished in highly state anxious women by OT administration.

The fact that the ratio of Attack to Earn responses shifted from above to below unity under OT treatment for high state anxiety participants suggests that OT may also be affecting attentional processes. Anxiety is associated with a lowered threshold for detecting threatening stimuli and difficulty in disengaging from them. This bias occurs at automatic and strategic levels of processing (Cisler & Koster, 2010). In our study, provocation by their opponent may have dominated the attention of more anxious participants resulting in less attention available for point-earning. If this is correct, then OT diminishes the perceived magnitude of the threat, allowing for greater attention to be allocated elsewhere. The amygdala is implicated in automatic attention to threat but communicates with the prefrontal cortex which controls attentional mechanisms. High attention to threat is associated with reduced prefrontal activity controlling task-relevant processing (Bishop, 2009). We note here that we used a measure of state anxiety, rather than trait anxiety as in previous studies. This not only adds plausibility to the above interpretation but operationally recognises that the effects of OT are temporary and situational: There is no expectation that OT alters underlying and enduring personality traits.

It seems then that OT reduced anxiety in the face of provocation in women high in state anxiety. This appears to run counter to the findings of Domes et al. (2010) and Lischke et al. (2012) of enhanced amygdala activation to threat in women following OT administration. Two solutions to this apparent anomaly present themselves. The first is that the relationship between amygdala activation and behavioural response correspond to different systems with different functions. OT has peripheral as well as central effects. Peripherally, after synthesis in the hypothalamus

and release from the posterior pituitary, OT acts as a hormone circulating in the bloodstream and capable of affecting target organs. Central amygdala activation may increase levels of peripheral OT which are responsible for autonomic relaxation (Grewen & Light, 2011) and constitute women's adaptive anti-stress response described by Taylor (2006; Taylor et al., 2000). In support of this, Lischke et al. (2012) found an increase in plasma OT levels following nasal administration. Other studies which have measured plasma OT responsiveness to stress have found that it is significantly increased in women with high levels of anxiety (Sanders, Freilicher, & Lightman, 1990). In women, central OT may target and sensitize the amygdala's alerting function which in turn triggers peripheral OT release, enhancing parasympathetic activity and reducing autonomic arousal.

A second possibility is that neuroimaging studies have not yet examined anxiety as a possible moderator of OT effects and, if high anxiety women were included, they would show a different pattern of results. In addition to correlating women's state anxiety with OT-responsive amygdala activation, it would be of considerable interest to include behavioural and peripheral measures. This would allow investigation of the relationships between OT, measures of central threat response (e.g. amygdala), autonomic reactivity (e.g. heart rate, skin conductance) and behaviour. Replication of the present aggression paradigm incorporating such measures would be helpful in clarifying how perceived threat, physiological reactivity and aggression are connected, and how they are modulated by OT.

Our results add to the increasing recognition that OT frequently interacts with other variables to produce its effects (Bartz et al., 2011). Anxiety is one of the most fundamental of personality traits and one that has been directly implicated in OT action. Our data indicate that OT reduces aggression among women high in state

anxiety. Further research on anxiety-based moderation of OT effects is needed for the development of theory as well as for identifying its potential applied value.

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